

eters, the detector 302 can communicate a signal to a controller 304 as to the type of particle passing through the detection region 284.

[0205] As a predetermined type of particle 292 passes through the detection region 284 and approaches the branch point, a controller 304 can, at the appropriate time, activate a change in a flow resistance associated with the first and second output channels 288, 286 using, for example, any of the microfluidic valves of the type discussed above. In one embodiment, a valve membrane or diaphragm 306 can expand under positive pressure into the second output channel 286 at the branch point, thereby increasing the resistance against the sample flow to prevent a tagged particle 292 from flowing into the second output channel 286. In the same way and at the appropriate time, a valve membrane or diaphragm 308 can expand under negative pressure out of or away from the first output channel 288 at the branch point, thereby decreasing the fluid resistance through the first output channel 288 and allowing the particle 292 to flow into the first output channel 288.

[0206] In another embodiment, the detection system can also include a Fluorescence Polarization (FP) system. A change in polarization of a particle tagged with a dye, over free dye, can enable gating and sorting of desired particles. Using FP, the tagged particles can further be separated on size differences because tagged particles with different sizes will exhibit different polarization values and can be differentially separated into individual outlets. A detector measures the FP value and signals the controller, which in turn changes the channel resistance appropriately, as described above, to direct the particles to an appropriate outlet.

[0207] As with the magnetic system of FIG. 15A, the fluorescence system of FIG. 15B can provide significant advantages over conventional systems. Because of the sharp focusing of particles, only slight changes of direction are needed to determine the direction of a particular particle, allowing for higher throughput with less noise. In addition, longitudinal ordering of particles significantly reduces noise as the system can more reliably distinguish the discrete positions of individual particles along the length of the channel and flow resistance changes in output branches can be more easily time for accuracy. So divided, the tagged particles 292, as well as any untagged particles, can be identified, sorted, counted, collected, and otherwise analyzed further as needed. A person skilled in the art will appreciate that any channel geometry can be used in this configuration, and any number of channels and channel branch points can be included to separate particle streams and perform sorting in parallel configurations.

[0208] In other embodiments, existing particle enumeration systems, for example flow cytometry, FACS, and/or MACS, can include a system of the invention to provide more accurate particle enumeration. A tightly focused stream of particles that is longitudinally ordered provides for extreme accuracy in the counting of particles of a predetermined type. Particles within a focused stream are ordered such that each particle can pass a predetermined point within an analytical region of a chip individually to be counted and analyzed, eliminating error due to clumping of particles.

[0209] In one embodiment, a system of the invention can be used to concentrate particles of a predetermined type from a dilute sample. Particles within a sample that are rare or dilute can be introduced into channels of the system having any geometry as noted above. The particles can be sorted and focused continuously and at high rates to achieve a concen-

trated sample in which the particles of a predetermined type are present with much higher frequency in a final sample in comparison to the original sample. Branches from a single channel and/or from multiple channels on a chip can be included to remove small volumes of focused particles from the original, dilute sample flowing within the channel to a collection reservoir containing the concentrated sample. A concentrated sample such as this can provide easier analysis and manipulation of rare particles and/or of particles that originate in a dilute sample.

[0210] Any number of system configurations can be provided for various applications, including sorting and counting as described above. Other system configurations can be designed to achieve certain specific results and/or properties associated with particle focusing within the various channel geometries. In the examples below, certain properties associated with the systems described herein will now be discussed in more detail. While certain experimental conditions may be discussed in reference to certain properties or parameters, it is to be understood that the properties and parameters are widely applicable to any of the channel geometries. Thus, a system of the invention can be configured in various ways for identifying, sorting, counting, and to achieve any number of the properties and parameters discussed in the examples below.

Example 1

[0211] Ordering and focusing of particles in the various channel geometries described herein is unaffected by relative particle density, as will be discussed in reference to FIGS. 16A-16C. When the density of the suspending solution is changed so that the suspended particles are either more or less dense than the solution (i.e., positive or negative buoyancy) focusing can be unperturbed and can remain at a consistent location, as illustrated in FIGS. 16A and 16B. For example, when particles both less dense (silicone oil, $\rho=0.95$ g/ml) and more dense (polystyrene, $\rho=1.05$ g/ml) than the suspending fluid ($\rho=1.00$ g/ml), are loaded simultaneously, both will focus to the same position, as shown in FIG. 16C. The independence of particle density for particle focusing is not consistent with a dominant centrifugal force acting directly on particles and suggests that Dean drag F_D is the dominant effect leading to symmetry reduction.

[0212] In particular, as noted in detail above, effects present in curving channels include (i) an inertial (centrifugal) force on suspended particles ($F_{\text{cf}}=\Delta m U_p^2/r$) and (ii) secondary rotational flows due to inertia of the fluid itself, Dean flow. For a constant geometry the average velocity of the Dean flow scales with the square of De . Two drag forces are considered that may act on suspended particles of radius, a , due to this secondary flow. Both viscous (Stokes) drag ($F_D=6\pi\eta a U_D$) and pressure drag [$F_p=(1/2)\rho\pi U_D^2 C_d a^2$] may be significant. Velocity conditions necessary for single focused streams allowed an order of magnitude calculation of the forces that may act in the system. For 10- μm particles in the range of channel velocities for successful focusing, F_p was <5% the magnitude of F_D , indicating that viscous drag (1-10 nN) is still more significant because of the small particle sizes. However, as the channel velocity increases, pressure drag may play a more dominant role because it increases with the fourth power of De , while viscous drag increases with only the square of De . This contribution may be significant for particle motion in higher velocity regimes, where focusing to multiple streams occurs. In the same successful focusing regimes cen-